In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 08-228V
May 31, 2011
To be Published

CATHERINE IRENE CORDER,	*	
	*	
Petitioner,	*	
	*	
v.	*	Entitlement; flu vaccine;
	*	Guillain-Barré syndrome;
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	four-month onset; Dr. Poser
	*	
Respondent.	*	

Travis T. Mohler, Morgantown, WV, for petitioner.
Lisa A. Watts, Washington, DC, for respondent.

MILLMAN, Special Master

DECISION[1]

Petitioner filed a petition[2] on March 28, 2008 under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that flu vaccine which she received on December 8, 2004 caused her Guillain-Barré syndrome (GBS) whose onset was April 6, 2005,

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would clearly be an unwarranted invasion of privacy. When such a decision is filed, petitioner has 14 days to identify and move to redact such information prior to the document's disclosure. If the special master, upon review, agrees that the identified material fits within the categories listed above, the special master shall redact such material from public access.

[2] Petitioner's husband George also filed as a petitioner, but since petitioner is an adult, alive, and not judged incompetent, the Vaccine Act does not permit George to file as a petitioner since he was not the vaccinee. Section 300aa-11(b)(1)(A) of 42 U.S.C. On January 4, 2008, the undersigned dismissed petitioner's husband as a petitioner.

four months after vaccination. The only issue in this case is whether flu vaccine can cause GBS four months later. The undersigned holds that it cannot.

FACTS

Petitioner was born on August 4, 1943. She is a retired registered nurse. Med. recs. at Ex. 1, p. 28.

On October 30, 2002, petitioner received influenza vaccine. Med. recs. at Ex. 1, p. 25.

On December 8, 2004, petitioner received influenza vaccine. Med. recs. at Ex. 1, pp. 3, 51.

On April 7, 2005, petitioner complained to her family doctor about arm and hand tingling and discoordination. Her legs felt very weak, her fingertips were numb, and she had tingling on both hands. Med. recs. at Ex. 1, p. 55. Her deep tendon reflexes in the lower extremities were intact and symmetrical. Id.

On April 7, 2005, at noon, petitioner went to the ER of Monongalia General Hospital, complaining of generalized weakness. She had vomited twice that day. Her husband had recently had bronchitis. Med. recs. at Ex. 2, p. 10.

On April 8, 2005, petitioner was admitted to Monongalia General Hospital and discharged on the same date to be transferred to Ruby Memorial Hospital. Med. recs. at Ex. 2, pp. 1, 16, 124. She had a rapidly evolving quadriparesis with ophthalmoplegia and bulbar palsy. Med. recs. at Ex. 2, p. 124. She first became ill on Wednesday, April 6, 2005. Id. She had very mild double vision. On April 7, 2005, she had ptosis of her left eyelid. On April 8, 2005, she developed weakness of her arms and then her legs. Id.

From April 9 to May 23, 2005, petitioner was at West Virginia University Hospitals. Med. recs. at Ex. 3, p. 1. She was diagnosed with GBS. Id.

On April 17, 2005, petitioner and her husband told hospital staff that she had had a flu vaccination within the last one to two months and had herpes simplex virus fever blisters within the last one to two months. Med. recs. at Ex. 3, p. 51.

TESTIMONY

Petitioner testified first. Tr. at 7. She denied that she had ever vomited on April 7, 2005. Tr. at 10. She does not remember having any herpes simplex virus fever blisters between the time she had her flu vaccination and her onset of GBS. Tr. at 11. She stated that the 2004 flu vaccination was her first one and denied that she had ever received flu vaccine in 2002. Tr. at 15.

Dr. John P. Conomy testified next for petitioner. Tr. at 17. He is a neurologist. Tr. at 18. Dr. Conomy is the sole owner of his neurologic practice, True North Medical Services. Tr. at 68. He is also a lawyer. Tr. at 22. He has never taken a bar examination and does not practice law. Tr. at 24. Dr. Conomy is also president of Health Systems Design, Inc., which is a consulting corporation he started in 1992, encompassing "the kinds of things that I do that draw upon medicine, occasionally upon the law, that do not involve the care of patients. Today's exercise is one of those things…." Tr. at 24. Dr. Conomy engages in consulting work, publications, seminar preparation, lecturing, etc. Tr. at 25. Health Systems Designs, Inc. is a one-man corporation. Id. Dr. Conomy looks at organizations of institutions and their staff all over the world and their need and capability for designing programs in education, research, and patient care. Tr. at 26. He obtains clients by networking. Id. Dr. Conomy is also president of CompEval Corporation which evaluates persons about whom a variety of agencies, private institutions, law practices, retirement organizations, and risk benefit organizations ask him to render an opinion about some aspect of the individual's health or capability, or both. Tr. at 26-

27. These individuals are not Dr. Conomy's patients. Tr. at 27. CompEval is a one-man corporation. Id. Between 10 and 15 percent of Dr. Conomy's professional time is devoted to evaluating people for various purposes that may end in a legal hearing. Tr. at 28. The rest of his time is dedicated to caring for his patients. Id. He devotes another 10 to 15 percent of his professional time to activities involving Health Systems Design, Inc. Tr. at 29. Putting the two corporations together, Dr. Conomy said that more likely 20 percent of his time is devoted to both. Id.

Dr. Conomy's opinion is that petitioner had GBS. Tr. at 40. He believes the most probable cause is the influenza vaccination. Tr. at 41. His basis is that since swine flu vaccine in 1976 was associated with GBS, other influenza vaccines may also cause GBS. Id. He stated that petitioner did not have any other illness to which to attribute her GBS. Tr. at 42. That she vomited in the emergency room does not constitute probable evidence for a disease in her intestinal tract. Id. He stated that cold sores are usually produced by immunologic memory rather than active infection. Tr. at 42-43. He admitted that generally people who develop GBS after receiving flu vaccines develop it sooner rather than later. Tr. at 43. "However, this does not exclude later as a possibility for that." Id. When challenged as to his opinion encompassing what is possible, rather than probable, Dr. Conomy corrected himself and said he meant "probability." Tr. at 43-44. He bases his opinion that flu vaccine can cause long-onset GBS on two articles: the Poser and Behan article, and the article published by the Massachusetts Department of Public Health Bureau of Communicable Disease Control in June 2006. Tr. at 45, 46. If GBS occurred one year after vaccination, it would not surprise Dr. Conomy that flu vaccine caused it. Tr. at 49. When asked if he thought the causal period would go out to 10 years, Dr. Conomy replied, "I think the longer one goes out the more improbable it becomes."

Id. When asked what his end point for causation is, he replied "I don't think there's any bright line." Id.

The Massachusetts document, which includes material from New Jersey, does not speak about a four-month onset but about a two-month onset. Tr. at 52. Dr. Conomy withdrew part of his basis in that he does not base his four-month opinion of causation on the Massachusetts and New Jersey state documents, but on the Poser and Behan article, and all the articles that Poser and Behan referenced in that article. Tr. at 54. The undersigned then ordered petitioner's counsel to file all the Poser and Behan referenced articles after the hearing. Tr. at 55.

When Dr. Conomy sees a patient who has GBS, he asks him or her "about diarrheal diseases, forms of enteritis, recent immunizations, illnesses of some kind that may have preceded this particular neurologic condition." Tr. at 61. When asked why he uses the word "recent" before "immunizations," Dr. Conomy said, "I want to know about ones that are, you know, particularly recent but perhaps ones that go back farther than that." Tr. at 62. When asked "farther than what," Dr. Conomy replied "Farther than the onset of this illness or the immediate weeks preceding it." Id.

Dr. Conomy's opinion is that petitioner's flu vaccine probably caused her GBS. Tr. at 63. He stated that one cannot put a cutoff date on an immune response, adding, "Bright lines tend to be arbitrary, and they're based on the practical need to make a cutoff date. They're not based on some scientific proof of some kind." Tr. at 65, 66.

Dr. Conomy admitted that in about two-thirds of GBS patients, the patients report a preceding infection within one to three weeks. Tr. at 70. He agreed that in one-third or more of GBS cases, no etiology of the GBS is ever determined. Tr. at 71. GBS is usually rapidly progressive. Tr. at 72. Because no serologic tests were performed on petitioner when she was

hospitalized in April 7 and 8, 2005, Dr. Conomy opined that we do not know whether she had a preceding infectious disease. Tr. at 75.

Dr. Conomy stated that petitioner's abnormal immune response began long before her clinical symptoms of GBS appeared, but he does not know when was the onset of her abnormal immune response. Tr. at 93, 94. Petitioner had no symptoms whatsoever between December 8, 2004 (the vaccination) and April 6, 2005. Tr. at 94-95. In the one case report upon which Poser and Behan rely in their article on long-onset GBS after vaccination, the individual in the case report had a low-grade fever, muscle aches, dizziness, and difficulty focusing one day after vaccination, symptoms which petitioner in this case did not have. Tr. at 97.

Dr. Thomas P. Leist, a neurologist, testified first for respondent. Tr. at 109. He specializes in neuroimmunological disorders and is on the faculty of the neurology department in Philadelphia. Tr. at 110. His opinion is that flu vaccine did not cause petitioner's GBS. Tr. at 112. His basis is that petitioner had a very uneventful course after receiving the vaccine. Id. She was seen by doctors between the date of her vaccination and the onset of her GBS in early April 2005, but none of these visits indicated any issues associated with her vaccination. Tr. at 112-13. The interval of four months is outside the time interval generally acceptable for an association between vaccination and GBS. Tr. at 113.

Furthermore, the medical records indicate that petitioner may have had nausea with vomiting as well as fever blisters closer in time to the onset of her GBS, which would be more proximate causes of her GBS than the vaccination. Id. In 35 percent of GBS cases, no approximate infectious or other event can be identified as the cause. Tr. at 115. No serology was done on petitioner, indicating that her doctors were not looking for a cause of her GBS. Tr. at 116. Epidemiologically, petitioner's onset interval of 16 or 17 weeks is well outside the

interval shown to be causative between swine flu vaccine in the Schonberger article and the Langmuir article. Tr. at 118. Normally, in GBS, the time interval is much tighter. With swine flu vaccine, there was a peak occurrence of one month post-vaccination when most GBS cases occurred. Tr. at 119.

Petitioner had previously received flu vaccine in 2002, which is two years before the vaccine at issue in this case. She did not have a reaction to her 2002 vaccination. Tr. at 120.

Poser's and Behan's article was published in 1982. Id. The article is an opinion piece by Dr. Poser primarily. Tr. at 121. From a modern understanding of immunology and what actually happens in GBS, Dr. Leist stated that the Poser and Behan article was a little bit dated even when it was published. Id. There is another explanation for why GBS patients have fluctuation of their neurologic symptoms after their initial event than the one Dr. Poser gave in his article. Id. Petitioner in this case has an illness that is not just demyelinating but also clearly axonopathic. Id. Over time, her neurons remyelinated but at different intermodal distances. Tr. at 122. The remyelinated neuron is not the same as a neuron that had not been demyelinated. Id. Very often, there are patients who, when they have febrile illnesses, will have fluctuations of their GBS symptoms. Id.

When Dr. Leist read the Poser and Behan article, he knew that it depicted an understanding of immunology at one point in time, but the article's claims would not stand up today based on the current understanding of immunology and of GBS. Id.

In two-thirds of GBS cases, there is an antecedent illness before onset, while in 35 percent of GBS cases, there is no report of an infection within three weeks. Tr. at 124. Antiganglioside antibodies are a pathophysiologically important component in many forms of GBS, and we can look for antiganglioside antibodies when some had campylobacter jejuni

infection. Tr. at 127. When looking for the etiology of GBS, one looks for an antecedent event within an appropriate time frame. Id. The swine flu vaccine epidemiologic studies were a seminal event because they gave the medical community enough cases to understand the risk periods. Tr. at 128. Dr. Leist's cut-off date for looking for risk is two to three months. Id. Langmuir indicates in his epidemiologic study that the time frame for risk of GBS after swine flu vaccine is six weeks when the risk returns to baseline. Tr. at 129. With campylobacter jejuni, the vast majority of the GBS occurs within the first two to three weeks. Id. An eight- to nine-week time frame is very conservative. Id. After a time interval of five to six weeks, the risk of GBS collapses very significantly. Id.

A killed virus vaccine, such as the flu vaccine, stimulates an immune response, but unlike chronic infections where the virus replicates in the body, a killed virus vaccine does not replicate. Tr. at 131. The reason doctors look at a two- to three-week interval after vaccination is because they question when the vaccine clears from the body. Id. If Dr. Leist had a patient who had GBS and reported an antecedent event three months earlier, he would rule out the three-month-old event as causal. Tr. at 133. He would say the same if the antecedent event were two-and-one-half months earlier. Tr. at 135. Dr. Leist does not subscribe to the idea that GBS lies dormant until it becomes clinical. Tr. at 142.

Dr. James L. Whitton testified next for respondent. Tr. at 157. He is both a medical doctor and a Ph.D. with expertise in virology. He is one of only eight editors on the journal Virology. Tr. at 158. He has published extensively in immunology. He has a laboratory which investigates immune responses in vivo. Tr. at 159. For six years, he has been on the review committee for the National Multiple Sclerosis Society. Id. He has done extensive work on vaccines and viruses. Tr. at 160.

Dr. Whitton's opinion is that petitioner's December 8, 2003 flu vaccination did not play any role in her development of GBS on April 6, 2005. Tr. at 162. His basis is the 17-week gap between vaccination and onset of GBS. Tr. at 163. He continued:

> [T]he 17-week gap between vaccination and the development of that disease is entirely inconsistent with the vaccine's having played a role in triggering the GBS. And I would say that there are at least two sub [sic] reasons for that.
> First of all, the primary response to vaccinations and to most infections is actually completed by one to three weeks. The acute phase is the response, and we call that the primary phase.
> That is consistent with the observation that the majority of cases of Guillain-Barré Syndrome which have been related to antecedent [events] occur within that one- to three-week window.
> That doesn't mean to say there's nothing beyond that window, but it's not extensively beyond that window, and the majority are about one to three weeks.
> So there's a nice overlap between what we know about the mammalian immune response and the occurrence of GBS which so far as we know is indeed an autoimmune disease. So that would be the first sub reason that the acute immune response simply doesn't last for 17 weeks. It lasts for about three weeks following vaccination.
> I will if asked later in the testimony give more information relevant to what Dr. Leist already mentioned which is that the immune responses to vaccines differ from those to infections and also the immune response to different vaccines differ[s] from one another. But that's a point of detail.
> The second reason is that even for a vaccine which was clearly associated with GBS which was as has been mentioned today the swine influenza vaccine given in 1976 …. where we have a very large population of individuals who received the vaccine, it's clear that the risk of GBS was extinguished by about six to eight weeks post vaccination.
> I provided in my expert report essentially a slightly modified reprint of the graphs, one of the figures from Langmuir at 1984. That's represented on page 7 of my report.
> I think that shows clearly that the risk of Guillain-Barré Syndrome declines within baseline levels by approximately eight or nine weeks after the reception of that vaccine. …
> The second point I would raise, and it's been made before, is that Mrs. Corder's medical records show clearly … that she encountered other possible triggers for GBS….

> Third, as also pointed out by Dr. Leist, Mrs. Corder is in the age group in which GBS most often develops. There's a higher baseline frequency of GBS in her age group.
> Fourth, she already has a preexisting autoimmune disease, autoimmune thyroiditis or Hashimoto's disease, and it's recognized that such diseases may predispose the development of GBS.

Tr. at 163-66.

Dr. Whitton continues with his list of reasons, including the fact that petitioner had an upper respiratory infection 21 weeks before the onset of her GBS. If Poser and Behan were correct that there is a long-onset GBS, then petitioner's upper respiratory infection four weeks before her vaccination should also be taken into account. Tr. at 167. If someone wanted to argue that a vaccine 17 weeks before onset is the trigger, then he should argue that an upper respiratory infection 21 weeks before onset is a more likely trigger. Id. Dr. Whitton stated there is no increased risk of GBS for influenza vaccines except for swine flu vaccine. Tr. at 167-68.

Petitioner received a killed virus vaccine. Tr. at 169. The components of that vaccine cannot replicate. Id. A subpart of the immune system develops influenza-specific immune responses. Id. These responses are antibody responses, not killer T-cell responses. Id. The immune response is divided into two general areas. One is termed the innate immune response while the other is termed the adaptive immune response. Tr. at 170. The adaptive response has memory. Id. The earliest part of the adaptive response probably is day three post-immunization. Tr. at 171. The primary response peaks around day 10, and then the immune response declines. Id. By the 21st day, the immune system enters into the memory phase. Id. Degradation of the vaccine proteins is a necessary part of the immune response so the adaptive immune system can recognize better the viral proteins. Tr. at 172.

In Dr. Conomy's second report, he mentions cellular immunity injuring nerve cells. Id. This was an idea popular 30 years ago to explain peripheral nervous system disease such as GBS, but it was debunked long ago. Tr. at 173. Cellular immunity involves T-cells and may be important in multiple sclerosis. Id. By contrast, for GBS, most current researchers think antibodies against gangliosides on the surface of peripheral nerve cells cause GBS. Id. There is no credible evidence that T-cells are involved in GBS. Tr. at 177. There is nothing in very extensive literature in animal research and in humans to support the contention that vaccination causes GBS in an individual 17 weeks later. Tr. at 174. If there were pre-existing T-cells around ganglia ready to develop GBS, such individuals would be likely to develop it very soon after exposure to a trigger, not 17 weeks later. Tr. at 177. That is the anamnestic response. Tr. at 178.

Poser and Behan were presenting a hypothesis in their article on long-onset GBS. Tr. at 175. It is almost three decades old and still not validated. Id. Poser and Behan's suggestion of the pathological process seems clearly wrong. They suggest that GBS causes deposition of antibody-antigen complexes resulting in vasculitis, a process for which they created the term vasculomyelinopathy. Id. Dr. Whitton stated that this is "not a term that has remained in scientific consciousness." Id. Their proposal in terms of pathogenesis underlying GBS is almost certainly wrong because the antibodies that appear to be agents of harm are antigen specific and do not involve vasculopathy. Id.

The Massachusetts release appended to Dr. Conomy's written report does not support petitioner's allegations. Tr. at 178. The document states that the incubation period is typically one to three weeks, with which Dr. Whitton agrees. Id. The authors of the release suggest that case investigators ask for antecedent events occurring only eight weeks before onset of GBS,

which makes good sense to Dr. Whitton. Tr. at 178-79. The New Jersey submission of May 2003 appended to Dr. Conomy's written report does not support petitioner's allegations. Tr. at 180. It discusses onset of GBS within two months following c. jejuni infection even though most cases following c. jejuni are acute. Tr. at 181.

That petitioner had vomiting before her GBS suggests a gastrointestinal infection, but even if there were no antecedent event other than her vaccination four months earlier, that does not mean the vaccine is the cause. Tr. at 183. A significant minority of GBS cases have no identifiable antecedent event. Id. Dr. Whitton stated that the time period of 17 weeks is "just inconsistent with any association of the vaccine or indeed of any triggering event and subsequent development of GBS at this very late time point." Id.

Other Submitted Material

Petitioner filed as Exhibit 17 her affidavit, stating that the onset of her GBS was April 6, 2005, when she woke in the middle of the night with weakness, tingling in her right arm and hand, and incoordination. Ex. 17, p. 2.

Petitioner filed as Exhibit 18 her husband's affidavit, stating that the onset of petitioner's GBS was the night of April 6, 2005 when she had generalized weakness and tingling in her extremities. Ex. 18, p. 1.

Petitioner's Expert Submitted Material

Petitioner filed as Exhibit 16 an affidavit of Dr. John P. Conomy. He states that petitioner's GBS vaccination on December 8, 2004 caused her GBS in early April 2005, but gives no basis for his opinion other than that GBS is an uncommon but known and recognized hazard of flu vaccination. Ex. 16, pp. 1-2.

Pursuant to the undersigned's Order that Dr. Conomy give a basis for his opinion that petitioner's flu vaccination caused her GBS four months later, petitioner filed an Addendum Report from Dr. Conomy, without giving it an exhibit number. He states:

> The autoimmune perturbations set in motion by vaccines (as well as other agents) by which sensitized immune cells attack the myelin membranes of peripheral nerves and their ganglia are set in motion long before a patient expresses weakness and other manifestation[s] of that condition. That incubation may be brief (days), intermediate (weeks) or long (months). …
> Long latencies between the reception of a likely offending or causative agent, extending up to months, are stated in the following learned reports regarding [GBS].

Addendum Rep., p. 1. In support of his opinion, Dr. Conomy lists an article by C.M. Poser and P.O. Behan entitled "Late Onset Guillain-Barré Syndrome," 3 J Immunol 27-41 (1982), and two state department of health publications, the first being the Massachusetts Department of Public Health, Bureau of Communicable Disease Control, publication entitled "Guillain-Barré Syndrome" (June 2006), 274-78, with two worksheets attached, and the second being the New Jersey Department of Health and Senior Services publication entitled "Guillain-Barre Syndrome" (May 2003), 1-4. Neither the Poser/Behan article nor the state health publications have exhibit numbers.

Also attached to Dr. Conomy's Addendum Report is his 38-page curriculum vitae dated September 2004. This also does not have an exhibit number. Dr. Conomy is both a neurologist and an attorney. He is president of a corporation called Health Systems Design, Inc., and of a corporation called CompEval Corporation. CV at 1. Dr. Conomy is also president of the corporation for which he practices neurology. CV at 2. He is board-certified in both neurology and forensic medicine. Id.

Poser and Behan begin their article on late-onset GBS with a summary, stating that GBS usually occurs within one month of a precipitating cause. 3 J Immunol 27. The authors' intent is to show that cases may occur weeks to months later and that the etiology of GBS is humoral rather than cell-mediated. Id.

Poser and Behan state, "The length of the latent period appears to be a good index of the severity of the disease: a short latent period (up to two weeks) was followed by a severe and fatal illness, while a long latent period was followed by a mild illness [citing article]." Id. at 28. In the instant action, petitioner's GBS is unfortunately very severe, indicating, according to Poser and Behan, a short latent period, the very opposite conclusion Dr. Conomy made purportedly based on this article.

Poser and Behan discuss animal experimentation to induce experimental allergic neuritis (EAN), an animal analogue to GBS, and experimental allergic encephalomyelitis (EAE), an animal analogue to MS, and assert animals may manifest symptoms up to a year after being injected with various substances. Id. at 31. They also posit that Dr. Poser's theory of a vascular process, which he coined vasculomyelinopathy, plays a role in GBS. Id. at 30. They discuss Dr. Behan's unpublished work describing the effect of using endotoxin on previously-sensitized animals to cause experimental allergic myasthenia gravis (EAMG) or EAE or EAN one year later. Id. at 31. They surmise that GBS and acute disseminated encephalomyelitis (ADEM) as well as EAN and EAE are all vasculopathies. Id. at 32.

Poser and Behan admit that the "documentation of patients who develop GBS after a long latent period is rare." Id. at 33. They explain this rarity by surmising that an infection or vaccination that occurred months before onset of GBS would be easily forgotten. Id. Then, the authors discuss subclinical GBS which occurs after the clinical GBS has run its course, with its

animal analogue, and theorize that the reverse of this process is "just as logical," i.e., that because subclinical GBS can occur after clinical GBS is over, subclinical GBS can also occur before clinical GBS even starts. Id. They state:

> Here again, the reverse situation is just as logical, i.e., that pathological changes may exist without symptoms prior to the development of acute GBS. We postulate that such a clinically silent, smouldering [sic] process may result from initial immunological attack and may become apparent much later as a result of an anamnestic response.

Id. That statement posits that there is a later anamnestic response. In the instant action, Dr. Conomy did not identify any later antigenic attack in petitioner's case to which she would have had an anamnestic response. He focused solely on her flu vaccination four months earlier as the cause of her GBS.

The authors continue their discussion of anamnestic response by reviewing literature that discusses individuals who had clinical GBS followed by smoldering. Id. at 34. None of these papers describes smoldering before onset of clinical GBS.

Poser and Behan then describe a case report of a 40-year-old postman who received swine flu vaccine on November 17, 1976. The following day, he had pain in his chest and abdomen, generalized muscles aches, dizziness, and difficulty focusing. His temperature was 100° F. The symptoms continued for two weeks, and, by mid-December, one month post-vaccination, he could no longer do his work and had difficulty rising from a squatting position. One month after that, or two months post-vaccination, he had paresthesias of the hands and feet. His symptomatology continued and, in September 1977, he was diagnosed with a diffuse polyneuropathy. Id. at 34-35. Poser and Behan state this is "typical" case of a smoldering, very slowly progressive but "unrecognized" case of GBS. Id. at 35. The authors never mention chronic inflammatory demyelinating polyneuropathy (CIDP). They state that an intercurrent

acute gastrointestinal infection nine months after vaccination exacerbated this polyneuropathy into an acute phase. However, they state the onset was approximately one month post-vaccination. Id. It is hard to determine how this case report substantiates a postulated long-onset GBS when the polyneuropathy in the postman began within one month of vaccination. Petitioner in the instant action had no symptoms of polyneuropathy until 17 weeks after her flu vaccination.

Poser and Behan close with a discussion of sensitization to components of flu vaccines from prior vaccinations, leading to an anamnestic response. Id. at 36. They say that "in certain circumstances a delay of up to a year may occur, between an antecedent event, e.g., vaccination, and the onset of GBS." Id. at 37. They postulate that individuals already sensitized to a variety of viruses may have an anamnestic response from a vaccination to produce acute, clinical GBS "after a variable interval." Id. Poser and Behan caution that they are issuing a hypothesis about how GBS works pathologically, including their theory of vasculomyelinopathy, and state, "The value of our suggestion is that it provides an explanation for the clinical, pathological and immunological facts in GBS including those cases which have a late onset." Id. at 38.

Besides the Poser and Behan article, Dr. Conomy states that the other basis for his opinion about long-onset GBS due to flu vaccine comes from the publications of state health departments in Massachusetts and New Jersey. However, both documents discuss an onset interval of a few weeks (Massachusetts) or up to only two months (New Jersey), not the four months involved in the instant action. In his testimony, Dr. Conomy admitted that neither state publication serves as a basis for his opinion that flu vaccine can cause the onset of GBS four months later.

In the Massachusetts Department of Public Health, Bureau of Communicable Disease Control, Guide to Surveillance, Reporting and Control, the publication describes GBS, stating that in "about 66% of cases, an antecedent infection (occurring in the days to weeks preceding GBS symptom onset) is believed to trigger an immune response that reacts with nerves. Respiratory and gastrointestinal infections are the most commonly reported antecedent events." Mass. DPH, p. 274. This publication does not support an opinion that onset can occur 17 weeks later. The publication continues, "If a preceding respiratory or gastrointestinal illness is identified, it typically occurs 1-3 weeks prior to the onset of GBS symptoms." Id. at 275.

In describing how to investigate a case of GBS, the local board of health in Massachusetts is directed to report any confirmed or suspected case. Id. at 276. The local board of health is instructed to "Record the history of illness, including whether or not the case had fever, respiratory illness, gastrointestinal illness, or immunizations within the eight weeks preceding GBS." Id.

The New Jersey Department of Health and Senior Services publication states on its first page, "GBS can develop during the 2 months following a symptomatic episode of *C. jejuni* gastrointestinal infection." The publication notes that studies from Sweden show the risk of developing GBS during the two months after *Campylobacter jejuni* infection are approximately 100 times higher than the risk in the general population. NJ DPH, p. 1. In instructing local health officers in New Jersey to report cases of GBS, the publication instructs:

> Accurately record the demographic information, date of symptom onset, whether hospitalized (and associated dates), outcome of disease, and whether the patient has any preceding infection (viral or bacterial, ask specifically about campylobacteriosis), vaccination or surgery in the past 2 months.

Id. at unnumbered 3.

Poser and Behan's References

At the hearing in this case, Dr. Conomy testified that the basis for his opinion on long-onset GBS was not only the Poser and Behan article, but also the articles which Poser and Behan referenced in their article. The undersigned ordered that petitioner file these articles, which petitioner did as Exhibits 1-87. (Poser and Behan actually referenced 93 articles.) The exhibits are arranged in alphabetical order, which matches Poser and Behan's reference list at page 38 of their article, but the exhibits are obviously not in the order in which Poser and Behan alluded to them within their article. For the sake of clarity, the undersigned will discuss them in the order in which Poser and Behan alluded to them, rather than in the numerical order in which petitioner filed them. Thus, the first article Poser and Behan referenced was Miller and Stanton, which is petitioner's Exhibit 51. (This is actually Poser and Behan's 55th reference in their list of references, but there is a difference in exhibit number compared to reference number due to the fact that petitioner filed only 87 of the 93 references.)

Poser and Behan first cite "Neurological sequelae of prophylactic inoculation" by H. Miller and J. Stanton, 23 Quart J Med 1-27 (1954), for the proposition that GBS looks the same regardless of its cause. The article is a much broader discussion of neurologic anomalies after numerous vaccinations, all of whose onsets occurred within days to a couple of weeks after vaccination. Ex. 51.

They then cite Poser's own article "Disseminated Vasculomyelinopathy. A Review of the Clinical and Pathologic Reactions of the Nervous System in Hyperergic Disease," 45 Acta Neur Scand Supp. 37:7-44 (1969), for the same proposition that GBS looks the same regardless of its cause. Ex. 55. In his article, Poser describes post-vaccinal encephalomyelitis and states that the incubation period is between eight and 15 days. Ex. 55, p. 14. He also describes post-vaccinal encephalopathy and states that the incubation period is between two and 18 days. Id. at 14-15.

He recounts literature showing, inter alia, cases of GBS after Salk polio vaccination, one occurring within hours of vaccination and the other occurring 23 days after vaccination. Id. at 16. He notes a man who died of cervical transverse myelopathy five weeks after receiving his second typhoid-paratyphoid-tetanus vaccination. Id. at 18. Poser describes a man who received repeated injections of lyophilized calf's brain extract to treat progressive left-sided hemiparkinsonian syndrome who developed sudden right hemiparesis 22 days after the seventh injection which led to his death. Id. at 22-23. He discusses a child who developed cerebral edema two weeks after chickenpox infection. Id. at 28. Poser notes a child who had weakness of arms and legs plus double vision whose onset was 10 days after he had a slight cold with chills. Id. at 34. Cerebral biopsy showed edema, which Poser considers to be part of GBS. Id.

For the proposition that a latent period of less than four weeks between antecedent event and onset of GBS is a basic tenet of neurology, Poser and Behan cite three articles. The first is "The Guillain-Barré Syndrome. Definition, Etiology, and Review of 1,100 Cases" by F. Leneman, 118 Arch Intern Med 139-44 (1966). Ex. 41. Of the 1,100 GBS cases the author reviewed, 365 had no antecedent or underlying illness, while 735 cases did. Id. at 141. The two-thirds of GBS cases with antecedent or underlying illness were not found to be etiologic in nature. Id. The author does not discuss onset intervals appropriate to a view of causation.

The second article Poser and Behan cite for the neurologic tenet of looking for an antecedent cause of GBS no longer than four weeks earlier than onset is "Guillain-Barré Syndrome. A 42-Year Epidemiologic and Clinical Study" by R.H. Kennedy, et al., 53 Mayo Clin Pro 93-99 (1978). Ex. 37. The authors describe GBS as a "rapidly ascending paralysis." Id. at 93. The authors looked at the Mayo Clinic central medical-records linkage system for the population of Olmsted County, Minnesota, over a 42-year period. Id. From a review of 4,500

records, the authors identified 40 GBS cases. Id. at 94. They describe GBS as "a subacutely evolving paralysis that usually reached a maximum in 1 to 3 weeks." Id. They checked all preceding (within four weeks) upper respiratory tract infections, febrile illnesses, and gastrointestinal symptoms for comparison with a control group. Id. The authors compared patients who had GBS with those who had Bell's Palsy as a control group. Id. Antecedent infections occurred in 28 of the 40 GBS patients within four weeks of onset of GBS. The time interval between illness and onset of GBS varied from less than one week to four weeks with a median of one week. Id. at 95. Those with antecedent infections had upper respiratory infection, gastrointestinal illnesses, febrile illnesses, or a combination thereof. Id. at 95-96. One had measles three weeks before the onset of GBS. None had immunizations. Id. at 96.

The third article which Poser and Behan reference for the neurologic tenet of looking for an antecedent cause of GBS no longer than four weeks earlier is "Epidemiology of Guillain-Barré syndrome" by D. Soffer, et al., 28 Neurology 686-90 (1978). Ex. 74. The authors selected patients for their study who fit the criteria of GBS including acute or subacute onset with evolution of signs within two months. Id. at 686. This article goes beyond the four weeks Poser and Behan mention in their article as the customary period during which doctors look for antecedent events.

On page 28 of the Poser and Behan article, Poser and Behan refer to the Schonberger, Langmuir, and Keenlyside articles for the proposition that epidemiological studies "appear to have established 12 weeks as an acceptable incubation period for acute GBS associated with the swine flu vaccination program." Actually, Schonberger and Langmuir wrote that the association ended at 10 weeks. Keenlyside's focus was not on duration of onset period but on fatalities.

The Schonberger article is petitioner's Exhibit 69 entitled "Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977" by L.B. Schonberger, et al., 110 Amer J Epidem 2:105-23 (1979). In 1976, the federal government sponsored the National influenza Immunization Program (NIIP) to vaccinate almost all adults and those children at high risk of serious illness from exposure to A/New Jersey influenza (also known as swine flu). Id. at 105. The program began on October 1, 1976 and included a nationwide surveillance system to detect any increased incidence of possible adverse reactions. By December 2, 1976, when 35 million vaccinations had been given, two clusters of GBS (in Minnesota and Alabama) were reported to the CDC. Id. at 105-06. By studying preliminary data from four states, CDC determined that there was a seven-fold increase in the incidence of GBS among vaccinees. Id. at 106. Case reports from the four states and seven others suggested an association between swine flu vaccination and onset of GBS two to three weeks later. The swine flu vaccination program was suspended on December 16, 1976 and GBS surveillance was expanded nationally, occasioning this article. Id.

The study period was from October 1, 1976 to January 31, 1977. Id. The peak relative risk of GBS after vaccination occurred in weeks two and three post-vaccination. Prior to the 10^{th} week after vaccination, all relative risks were significantly greater than 1 with a 95% confidence interval. Id. After the 10^{th} week post-vaccination, the relative risk of GBS was not significantly different than 1. Id. The unvaccinated GBS patients reported a significantly greater frequency of acute illness in the four weeks prior to onset, 61.8%, compared to the rate of prior acute illness, 32.8%, in the vaccinated GBS patients. Id. at 116. This difference in the rate of prior acute illness plus the occurrence of most GBS cases within four weeks of vaccination suggested to the authors that the vaccine triggered the GBS. Id. at 120, 121. The authors discuss GBS:

"GBS represents an immunopathologic reaction, triggered by recent exposure to an exogenous agent." Id. at 122.

The Langmuir article is petitioner's Exhibit 41 entitled "Guillain-Barré syndrome: the swine influenza virus vaccine incident in the United States of America, 1976-77: preliminary communication" by A.D. Langmuir, 72 J Royal Soc of Med 660-69 (1979). One statistically significant difference between the vaccinated GBS group and the unvaccinated controls was the higher proportion in the unvaccinated controls of an acute illness during the four weeks prior to onset of GBS. Id. at 663. The peak of GBS cases in the vaccinated group was in the third week after vaccination. Id. at 664. Some increased risk of GBS post-vaccination remained discernible up to the 10th week. Id.

The Keenlyside article is petitioner's Exhibit 36 entitled ""Fatal Guillain-Barré syndrome after the national influenza immunization program" by R.A. Keenlyside, et al., 30 Neurology 929-33 (1980). In most cases (77%), onset of GBS symptoms began within four weeks post-vaccination. Id. at 930.

Poser and Behan quote from Knox on page 28 of their article that the latency or onset period varies from a few days to two months and that the length of the latency period appears to be a good index of the severity of the GBS. A latency period up to two weeks was followed by severe and fatal illness while a long latency period was followed by a mild illness. This would go against petitioner's expert's Dr. Conomy's opinion in the instant action since petitioner unfortunately has a very severe case of GBS with axonal involvement yet her latency period is long, i.e., four months. If Knox were correct (and willing to extend the latency period beyond his limit of two months to four months), petitioner should have had a mild case of GBS.

The Knox article is petitioner's Exhibit 40 entitled "Herpes Zoster and the Landry-Guillain-Barre Syndrome" by JDE Knox, et al., 24 J Neurol Neurosurg Psychiat 167-72 (1961). The article is based on three case reports. The first had an interval one month between herpes zoster and onset of left hand numbness. Id. at 167. The second had an interval of six weeks between herpes zoster and gradual loss of power in both legs with tingling in both feet. Id. at 168. The third had an interval of seven weeks between herpes zoster and weakness in the left leg. Id. at 169. In describing 10 other articles and their own three case reports reflected in Table III of the article, the authors comment that the latency period varied from a few days to two months. Id. at 170. "The length of the latent period appears to be a good index of the severity of the disease: a short latent period (up to two weeks) was followed by a severe and fatal illness, while a long latent period (two weeks to two months) was followed by a mild illness." Id.

Poser and Behan also mention Gilmartin on page 28 of their article who described a latency period of two to 14 weeks between rubella vaccination and myeloradiculoneuropathy. The Gilmartin article is petitioner's Exhibit 25 entitled "Rubella vaccine myeloradiculoneuritis" by R.C. Gilmartin, et al., 80 J Ped 3:406-12 (1972). The mean latency period was 39 days or just over six weeks. Id. at 407.

On page 28 of their article, Poser and Behan continue their discussion with reference to the theory of cellular immune mechanisms, mentioning articles by Knowles and Behan (this is the same Behan who is co-author of the article by Poser and Behan). The Knowles article is petitioner's Exhibit 39 entitled "Preliminary Communication. Lymphocyte Transformation in the Guillain-Barré Syndrome" by M. Knowles, et al., 2 Lancet 1168-70 (1969). The authors studied seven patients, five of whom had an upper respiratory infection from one to four weeks prior to onset of GBS. Id. at 1168. The Behan article is petitioner's Exhibit 5 entitled "Cell-Mediated

Hypersensitivity to Neural Antigens. Occurrence in Human Patients and Nonhuman Primates With Neurological Diseases" by P.O. Behan, et al., 27 Arch Neurol 145-52 (1972). As part of their study, the authors immunized primates to produce experimental allergic neuritis, which usually started between days 14 and 20 after immunization. Id. at 149. They also produced experimental allergic encephalomyelitis in two monkeys whose onset was days 11 and 16 after immunization. Id. at 149-50.

Continuing their discussion of the pathology of GBS, Poser and Behan on page 29 of their article refer to two papers by Saida. The first Saida article (with Kyoko Saida as the primary author) is petitioner's Exhibit 66 entitled "*In Vivo* Demyelination Induced by Intraneural Injection of Anti-Galactocerebroside Serum. A Morphologic Study" by K. Saida, et al., 95 Am J Pathol 99-116 (1979). By injecting rabbit anti-galactocerebroside serum into the sciatic nerves of rats, the authors were able to induce demyelination, with changes in morphology 20 minutes after inoculation. Id. at 103. After five days, most nerve fibers within the lesion were completely demyelinated. Id. at 104. The second Saida study (with Takahiko Saida as the primary author) is petitioner's Exhibit 67 entitled "Experimental Allergic Neuritis Induced by Sensitization with Galactocerebroside" by T. Saida, et al., 204 Science 1103-06 (1979). The authors caused the first successful production of experimental allergic neuritis (EAN) in rabbits by repeatedly immunizing them seven or eight times with galactocerebroside (GC). Id. at 1103. Onset of EAN in 13 of 31 rabbits ranged from day 44 (6 weeks) to day 314 (11 months) after the first inoculation. Id. The mean onset was 135 days (4.8 months) plus or minus 21 days (three weeks). Id. There were three immunization schedules for the rabbits. The first schedule was intramuscular injections at four sites on the back monthly for the first four injections, and then every three months thereafter for up to a year. The second schedule was intramuscular injections

every two weeks for the first three injections and intraperitoneal injections every three to four weeks after that for up to seven months. The third was intradermal injections at four foot pads for the first injection, weekly for the three successive intramuscular injections, and thereafter intraperitoneal injections six times until day 130 after the first sensitization. Control rabbits for each group were inoculated with the same procedure as to timing and number of injections, but omitting GC from the injection. Id. at 1105 (Table 1).

Continuing on page 29 of their article their discussion of the pathology of GBS, Poser and Behan refer to studies by Gilpin, Scheinker, Prineas, and Behan (the co-author of the Poser and Behan article).

The Gilpin article is petitioner's Exhibit 26 entitled "Polyneuritis. A Clinical and Pathological Study of a Special Group of Cases Frequently Referred to as Instances of Neuronitis" by S.F. Gilpin, et al., 35 Arch Neur Psych 5:937-63 (1936). The authors studied a series of cases of polyneuritis over 15 years at the Mayo Clinic. Id. at 937. They designate these cases as neuronitis rather than polyneuritis. Id. Of the 20 cases under consideration, 60 percent had a prior infection, usually influenza or an upper respiratory infection. Id. at 940. The latency period varied from a few days to several months with the average latency period being seven weeks. Id. The authors state that just because all the patients did not give a history of a prior infection does not mean they did not have a prior infection. Id. The authors conclude that "we are dealing with a condition due to a virus that … has a predilection for the peripheral neurons." Id. at 958-59.

The Scheinker article is petitioner's Exhibit 68 entitled "Pathology and Pathogenesis of Infectious Polyneuritis" by M. Scheinker, 72 Trans Amer Neurol Assoc 141-43 (1947). The author studied 10 fatal cases of infectious polyneuritis and found tremendous swelling of the

nerve fibers of the spinal cord roots. Id. at 141. After the author's findings, he has a written discussion with others over whether destruction of myelin was primary. Dr. Scheinker thought it was not; his interlocutors thought it was. Id. at 142-43.

The Prineas article is petitioner's Exhibit 60 entitled "Pathology of the Guillain-Barré Syndrome" by J.W. Prineas, et al., 9 Ann Neurol (suppl.) 6-19 (1981). The authors note that chronic relapsing polyneuritis differs from GBS (categorized as acute idiopathic polyneuritis) because chronic relapsing polyneuritis has a relapsing course and often a slower onset. Id. at 9 and Table.

The Behan article is petitioner's Exhibit 8 entitled "Immunopathological Mechanisms of Allergic Neuritis in Animals, Primates, and Man" by P.O. Behan, et al., 94 Trans Amer Neurol Assoc 219-24 (1969). The authors induced allergic neuritis in rabbits, monkeys, and baboons with human sciatic nerve and/or an extract of human peripheral nerve in complete Freund's adjuvant, and then did in vitro testing on the cells. Id. at 220. They also had access to nine human patients with GBS. Id. Abnormal cells were found on the fourth day post-immunization in animals and the sixth day post-infection in humans. Id. at 221. By the 56th day (or eighth week), the number of abnormal cells in both primates and humans decreased to normal. Id. Maximal stimulation was observed with cells taken from experimental animals on the 30th day post-immunization. Id. Similarly, lymphocytes taken from patients had their greatest lymphocytic reaction about 30 days after apparent infection. Id. In both primates and humans, the degree of response declined by the 56th day (or eighth week). Id.

Poser and Behan continue their discussion of pathology of GBS by referring to the Caspary, Walls, Schröder and Krücke, Allt, and Behan articles on Poser and Behan's page 29. The Caspary article is petitioner's Exhibit 14 entitled "Sensitized lymphocytes in muscular

dystrophy: evidence for a neural factor in pathogenesis" by E.A. Caspary, et al., 34 J Neurol Neurosurg Psychiat 353-56 (1971). The authors compare muscular dystrophy, a genetic disease, with GBS. In GBS, lymphocytes responded to muscle antigen less than to protein of the central or peripheral nervous system. The reverse was true in preclinical muscular dystrophy where there is well marked sensitization to neural antigens before establishment of clinical disease. Id. at 355.

The Walls article is petitioner's Exhibit 82 entitled "Cellular hypersensitivity to brain antigen in children of a family with hereditary ataxia" by R.S. Walls, et al., 42 J Neurol Neurosurg Psychiat 203-07 (1979). As in muscular dystrophy, a genetic disease, so in hereditary ataxia, immunologic reactivity may precede clinical expression of the disease. Id. at 203. Some have theorized that hypersensitivity to peripheral nerve antigens may precede clinical onset in GBS. Id. at 305.

Petitioner did not file the Schröder and Krücke article: "Zur Feinstruktur der experimentell-allergischen Neuritis beim Kanichen," 14 Acta Neuropath (Berl) 261-83 (1970).

The Allt article is petitioner's Exhibit 2 entitled "The Vulnerability of Immature Rabbits to Experimental Allergic Neuritis: A Light and Electron Microscope Study" by G. Allt, et al., 29 Brain Research 271-91 (1971). The authors injected human sciatic nerve with Freund's complete adjuvant into the left hind foot pad of rabbits older than two weeks and into the left and right hind foot pads of rabbits younger than two weeks. Id. at 272. The mean day of onset was 21 days (or three weeks) plus or minus 13 days whereas in older rabbits, the mean was 16.1 days (or two and one-half weeks) plus or minus 5.7 days. Id. at 274-75.

On page 30 of their article, Poser and Behan discuss Poser's thesis that there is a vascular component of GBS, referring to the article by Schaltenbrand and Bammer. However petitioner

did not file the Schaltenbrand and Bammer article: "La clinique et le traitement des polynévrites inflammatoires ou séreuses aiguës," 115 Rev Neurol 783-810 (1966). Petitioner did file the Ala and Shearman article (regarding vascular component of GBS) as Exhibit 1 entitled "Autoimmune Haemolytic Anaemia, Thrombocytopenia and Landry-Guillain-Barré Syndrome" by F.A. Ala and D.J.C. Shearman, 34 Acta haemat 6:361-69 (1965). The authors describe a man who had autoimmune hemolytic anemia and then two episodes of GBS who subsequently died. They posit that the patient may have been in an allergic state. Id. at 365. The patient represents multiple autoimmunity. Id. at 366.

Poser and Behan switch to analogizing GBS and acute disseminated encephalomyelitis (ADEM) on page 30 of their article referring to articles by Behan and Currie, Behan and Behan, Shiraki and Otani, Miller and Evans, Durston and Milnes, Yahr and Lobo-Antunes, Behan, Callaghan, and Poser.

The Behan and Currie chapter is petitioner's Exhibit 12 which is entitled "Acute Disseminated Encephalomyelitis," chapter four in Clinical Neuroimmunology (1978) 49-60. ADEM involves the white matter of the brain and spinal cord. Id. at 49. The authors note, "Clinical signs usually begin from seven to 21 days after the inciting event, whether it is an exanthem or immunization." Id. at 50. They repeat: "In the vast majority of cases of ADEM, there is a latent period of days to three weeks following the inciting event. This latent period is similar to the time between immunizing a susceptible animal with encephalitogenic material in adjuvant and the development of experimental allergic encephalomyelitis (EAE). EAE is the best known and most studied model of neuroallergy." Id. at 56.

Behan and Behan is a letter petitioner filed as Exhibit 87 entitled "Insect-sting encephalopathy" by P.O. Behan and W.M.H. Behan, 284 BMJ 504-05 (1982). They note that GBS can start after a bee sting. Id. at 505.

The Shiraki and Otani chapter is petitioner's Exhibit 72 entitled "Clinical and Pathological Features of Rabies Post-Vaccinal Encephalomyelitis in Man (Relationship to Multiple Sclerosis and to Experimental 'Allergic' Encephalomyelitis in Animals)" by H. Shiraki and S. Otani, chapter 2 in "Allergic" Encephalomyelitis. Proceedings of a Symposium: Experimental 'Allergic' Encephalomyelitis and its Relation to Other Diseases of Man and Animals" eds. M.W. Kies and E.C. Alvord (1959), 58-129. In 10 cases of post-rabies vaccination induced encephalomyelitis, the onset interval between the first vaccination and prodromal symptoms ranged from 7 days (one week) to 98 days (14 weeks). Id. at 60 (Table I). In the majority of delayed onset cases, 18 inoculations of attenuated live vaccine or of both attenuated live and inactivated vaccines were given. Id. at 64. The delayed cerebral form of central nervous system disturbances after antirabies inoculation with attenuated live vaccine occurred in Japan but not in Europe or the United States. Id. at 70. The authors attribute rabies post-vaccinal encephalomyelitis to repeated inoculation of antirabies vaccine. Id. at 112.

The Miller and Evans article is petitioner's Exhibit 50 entitled "Prognosis in Acute Disseminated Encephalomyelitis; with a Note on Neuromyelitis Optica" by H.G. Miller and M.J. Evans, 23 Quarterly J Med (New Ser.) 87:347-79 (1953). The authors studied 27 patients who had acute encephalomyelitis between 1932 and 1942. Id. at 348. Several of the patients gave a history of an immediately preceding non-specific illness, usually an upper respiratory tract infection. Id. at 349. The authors state this is a polymorphic illness (encephalitis, myelitis, encephalomyelitis, encephalomyeloradiculitis) which may be encountered in identical clinical

contexts: nine to 12 days after smallpox vaccination, on the fourth to sixth day of measles, "or rapidly following apparently non-specific upper respiratory infections." Id. at 369.

The Durston and Milnes article is petitioner's Exhibit 19 entitled "Relapsing Encephalomyelitis" by J.H.J. Durston and J.N. Milnes, 93 Brain 715-30 (1970). The authors discuss seven patients who had relapsing encephalomyelitis. Four had a preceding history of upper respiratory tract infection. Id. at 727.

The Yahr and Lobo-Antunes "brief communication" is petitioner's Exhibit 85 entitled "Relapsing Encephalomyelitis Following the Use of Influenza Vaccine" by M.D. Yahr and J. Lobo-Antunes, 27 Arch Neurol 182-83 (1972). They describe a 25-year-old woman who became febrile with headache and malaise two days after receiving her third influenza vaccine. Id. at 182. Six days after vaccination, she had vertigo, nausea, neck pain, and recurring headache. Id. A few days after that, she was confused, disoriented, and markedly ataxic. Her speech was slurred and she had difficulty using her left hand. Id. She was hospitalized and treated. For eight weeks she was well when she had a relapse. Id. The authors surmise that this is an autoimmune response and that the woman's two prior influenza vaccinations may have sensitized her to the subsequent third influenza vaccination. Id. at 183.

The Behan letter is petitioner's Exhibit 10 entitled "Diffuse myelitis associated with rubella vaccine" by P.O. Behan, I BMJ 166 (1977). Behan describes a 27-year-old woman who had paresthesias of both legs with increased reflexes eight days after she was vaccinated with live rubella virus. She was treated for a week, and recovered over the next six weeks followed by a relapse of left optic neuritis. Id. She was treated and recovered followed eight months later by another relapse of leg paresthesias which occurred one week after she had been exposed to children who had rubella. She recovered over the next six weeks. Behan states that her attacks

had been precipitated twice by exposure to rubella virus, the first by vaccination and the second by contact with children who had rubella. Id.

The Callaghan article is petitioner's Exhibit 13 entitled "Short Report. Relapsing neurological disorder associated with rubella virus infection in two sisters" by N. Callaghan, et al., 40 J Neurol Neurosurg Psychiat 1117-19 (1977). This is a case report of two sisters who had relapsing neurological disorders. Id. at 1117. One had onset five days after a flu-like illness. The other had onset seven days before the other sister did. Id. at 1118. Both sisters had a significant increase in the serum levels of rubella specific IgM indicating persistent infection. Id. at 1117. The authors state, "The short interval between the onset of symptoms in both sisters would be compatible with recent exposure to the rubella virus in both cases." Id. at 1118.

The Poser article is petitioner's Exhibit 56 entitled "Recurrent Disseminated Vasculomyelinopathy" by C.M. Poser, et al., 35 Arch Neurol 166-70 (1978). The authors discuss two cases of children who had neurologic difficulties, the first being a three-month-old girl with onset of left hemiplegia five days after an upper respiratory infection. Id. at 166. The baby recovered after treatment, but four months later, she contracted chickenpox and, five days after her first chickenpox lesions appeared, she had left arm weakness diagnosed again as left hemiplegia with left face and arm involvement. Id. The baby recovered after treatment, but one month later, three days after she had a mild cold, she stopped using her left arm. She was treated and recovered. Id. The second case child was a six-year-old boy who was hospitalized with sudden fever and massive left hemiplegia. Id. at 167. For the next four and ½ years, the boy continued to improve, but he was rehospitalized with fever, headache, confusion, somnolence, and slurred speech three days after he had been vomiting with a high fever. Id. Four years later, the boy was rehospitalized because of fever, headache, neck stiffness, and somnolence. Id. A

spinal tap showed gram-negative diplococci and he was diagnosed with meningococcal meningitis. Id. Two years after that, the boy was rehospitalized with fever, headache, nausea, vomiting, somnolence, and neck stiffness which occurred 18 days after he received swine flu vaccine. Id. He was diagnosed with acute hemorrhagic leukoencephalopathy and GBS following swine flu vaccination. Id.

Poser and Behan continue their discussion of animal models, including experimental allergic encephalitis or EAE, on page 30 of their article. They refer to articles by Wiśniewski, Alvord, Kadlubowski and Hughes, Hochberg, and Caspary. The Wiśniewski article is petitioner's Exhibit 83 entitled "An Ultrastructural Study of Experimental Demyelination and Remyelination. I. Acute Experimental Allergic Encephalomyelitis in the Peripheral Nervous System" by H. Wiśniewski, et al., 21 Lab Investigation 2:105-18 (1969). The authors injected rabbits with bovine brain white matter and complete Freund's adjuvant. Id. at 105. From 13 to 17 days later, they sacrificed four animals, examined their nerve roots, and found myelin destruction. Id. at 106. Interestingly, the authors comment on the repeated failure to induce demyelinating disease in normal animals by transferring massive doses of serum from animals with EAE suggests "that if a tag is involved it must act only over a short range, that is, …if it is present in the circulation it is rapidly absorbed by the target tissue…." Id. at 115.

The Alvord chapter is petitioner's Exhibit 3 entitled "Acute disseminated encephalomyelitis and 'allergic' neuro-encephalopathies" by E.C. Alvord, chapter 19 of Handbook of Clinical Neurology, vol. 9 (1970) 500-71. Alvord states that acute disseminated encephalomyelitis is an allergic reaction with hypersensitivity to one or a few central nervous system-specific antigens. Id. at 500. Investigators suspect that other diseases such as GBS may also be allergic. Id. He states, "In ordinary experimental allergic encephalomyelitis, produced

by the single injection of basic protein in Freund's complete adjuvant in guinea pigs, the antibody response is very small … and the sensitized lymphocyte response very large, as manifest by the development of delayed-type skin reactions to basic protein … beginning at 4 days and reaching a peak at 10 days…, followed in a few days by the development of experimental allergic encephalomyelitis." Id. at 517. Alvord notes that antigen can persist as "long" as three weeks before adjuvant is injected into the same site in the animal to evoke experimental allergic encephalomyelitis two weeks later. Id. at 523. Alvord describes the late form of rabies postvaccinal encephalitis in humans from a vaccine containing attenuated live virus. The latency period of the cerebral form was 35 days on average, much longer than the average of 15 days for the spinal form. Id. at 538-39. The occurrence of neural complications after measles and vaccinia is on average four to six days after the appearance of the rash and 11 to 13 days after vaccination. Id. at 546. Alvord states that postvaccinal (rabies and typhoid-paratyphoid) and postserum monoradiculitis commonly occurs seven to 10 days following serum, and rarely about three days after the second injection of typhoid-paratyphoid vaccine. Id. at 550.

The Kadlubowski and Hughes article is petitioner's Exhibit 35 entitled "The Neurogenicity and Encephalitogenicity of P_2 in the Rat, Guinea-Pig and Rabbit" by M. Kadlubowski and R.A.C. Hughes, 48 J Neurol Sci 171-78 (1980). Rats had onset of disease from 11-14 days. Id. at 173. Guinea-pigs had onset from 16-27 days. Id. at 174. Rabbits had onset on the 10^{th} day. Id. The rats produced pure experimental allergic neuritis (EAN) in reaction to bovine and human substances. Id. at 175. The guinea-pig did not produce EAN but did produce mild experimental allergic encephalomyelitis to the same substances. Id. The rabbit produced mild neuritogenic and encephalitogenic illness. Id. at 176.

The Hochberg abstract looks like a poster presentation at a conference and is petitioner's Exhibit 32 entitled "Recurrent EAE induced by *Herpes Simplex* Virus Infection" by F.H. Hochber, et al., 24 Neurology 384 (1974). They experimented on 25 rats, first inoculating their brains with herpes simplex virus, causing encephalitis, and, 10 days after the first injection, inoculating them again this time with guinea-pig spinal cord. The rats had typical experimental autoallergic encephalomyelitis (EAE) 10 to 14 days after the second injection. Id. Thirty days after the second injection, the authors injected the rats again with herpes simplex virus. Within 10 days of that third injection, six of the 25 rats had a recurrence of EAE. Their aim was to show that viral infection can reactivate EAE. Id.

The Caspary article is petitioner's Exhibit 15 entitled "Effect of Live Attenuated Vaccines on the Course of Experimental Allergic Encephalomyelitis. A Pilot Study" by E.A. Caspary, 16 Eur Neurol 176-80 (1977). The author injected groups of five guinea pigs with various attenuated viral vaccines and, two weeks later, challenged them with spinal cord and Freund's complete adjuvant to produce EAE. Id. at 176-77. The severity of their EAE depended on the type of attenuated viral vaccine the guinea pigs received prior to the injections with spinal cord. Id. at 177.

Poser and Behan mention more articles on page 31 of their article by Levine and Wenk, and Vogel. The Levine and Wenk article is petitioner's Exhibit 45 entitled "Exacerbation and Transformation of Allergic Encephalomyelitis by Pertussis Vaccine" by S. Levine and E.J. Wenk, 122 Proc Soc Exp Bio Med 1:115-18 (1966). The authors attempted to simulate multiple sclerosis in 75 rats by injecting their brains with guinea pig spinal cord to cause EAE. Id. at 115. Thirty-seven of the injected rats developed clinical signs of EAE after eight to 13 days. Id. Within two days, they were treated with either pertussis vaccine, typhoid vaccine, or nothing. Id.

An exacerbation of clinical signs occurred within two days, fully developed within another one to two days, in four rats that received pertussis vaccine. Id. at 116. Lesions of the relapse differed from those of the original attack of EAE. Id. at 117.

The Vogel article is petitioner's Exhibit 79 entitled "Treatment of Experimental Allergic Encephalomyelitis in the Rabbit" by C. Vogel, et al., 26 Arch Neur 1:366-73 (1972). The authors discuss experimental allergic encephalomyelitis (EAE), stating that two to three weeks after injecting an animal with whole central nervous system tissue, the animal has clinical signs of EAE. Id. at 366. The authors then experimented with various steroid treatments of the rabbits. Id. at 372-73.

Poser and Behan then switch to a discussion of animal experiments which they claim justify a long-onset association of vaccination and neurologic reaction in their article on page 31, referring to articles by Raine (guinea pigs without clinical signs for more than 12 months and clinical disease in other animals at 17, 35, and 50 weeks), Ravkina (clinical signs after 92 days in one monkey and 410 days in another), Sherwin (after repeated injections of sciatic nerve, onset of polyneuroathy six and one-half months later in one rabbit), Saida (onset of experimental allergic neuritis two to 11 months after injection).

What Poser and Behan omit from their discussion about long-onset association of vaccination and neurologic reaction is that Raine found chronic EAE only in immature guinea pigs. In adult guinea pigs, the onset of EAE was two to three weeks after injection with spinal cord mixed with complete Freund's adjuvant. The Raine article is petitioner's Exhibit 62 entitled "Chronic Experimental Allergic Encephalomyelitis in Inbred Guinea Pigs. An Ultrastructural Study" by C.S. Raine, et al., 31 Lab Invest 4:369-80 (1974). The authors discuss that, prior to the addition of adjuvants, scientists used to induce EAE by repeated administration

of injections to monkeys over several months. With the use of adjuvant, that repeated administration was no longer necessary and onset would occur in two weeks. Id. at 369. Using spinal cord with Freund's adjuvant incorporating mycobacterium tuberculosis, the authors inoculated the necks of 12 adult guinea pigs to produce acute EAE and nine juvenile guinea pigs to produce chronic EAE. Id. at 370. With the exception of one adult guinea pig who had no clinical signs, the 11 other adult guinea pigs had clinical signs of EAE from 14 to 18 days after injection. Id. With the exception of two juvenile guinea pigs who had no clinical signs, the other seven juvenile guinea pigs had onset from eight to 21 weeks after injection. Id. at 371. In attempting to explain why juvenile guinea pigs have such a long latency in comparison with the short onset interval of adult guinea pigs so that the former contract chronic EAE whereas the latter contract acute EAE, the authors state "there may be a threshold phenomenon associated with the degree or stage of myelination or immunocompetence…. One significant observation emanating from studies involving age-dependent disease responses is that guinea pigs, sensitized prior to the maturation of the CNS (*viz*. myelination and blood-brain barrier) and possibly of the immune system, develop chronic disease with a protracted course." Id. at 379. They note that animals such as the rat who are born with no central nervous system (CNS) myelin have no disease response after sensitization with CNS antigen. Id. The authors view chronic EAE as an animal model for multiple sclerosis. Id.

Poser and Behan also do not mention that the Ravkina article discusses juvenile animals, here young rhesus monkeys induced to have chronic EAE. The Ravkina article is petitioner's Exhibit 63 entitled "Chronic Experimental Allergic Encephalomyelitis in Rhesus Monkeys and its Modification by Treatment" by L. Ravkina, et al., 38 J Neurol Sci 3:281-93 (1978). The authors note that acute EAE is an animal analogue for postvaccinal encephalomyelitis whereas

multiple sclerosis needs a chronic EAE model. Id. at 281. They injected 24 young rhesus monkeys with spinal cord, vaseline oil, and dead BCG mycobacteria. Id. at 282. Each monkey received from three to 10 injections over a span of time. Id. Twenty-two of the 24 monkeys developed EAE, seven of them acute EAE and 15 chronic progressive EAE. Id. at 282, 285. The onset interval for the acute EAE was 20 to 39 days. Id. at 283. The onset interval for the chronic EAE was 34 to 410 days with most monkeys having onset between 34 to 48 days. Id.

The Sherwin article is petitioner's Exhibit 71 entitled "Chronic Allergic Neuropathy in the Rabbit" by A.L. Sherwin, 15 Arch Neurol 289-93 (1966). Sherwin notes that acute experimental allergic neuropathy (EAN) is the animal analogue to GBS. Id. at 289. In order to mimic cases of GBS which are followed by a relapsing and remitting course, Sherwin endeavored to reproduce a more chronic form of neuropathy by monthly injections of human sciatic nerve in Freund's complete adjuvant. Id. In some experiments, Sherwin used bovine, instead of human, sciatic nerve. Id. Fifteen rabbits received the first injection of human sciatic nerve in Freund's complete adjuvant, followed one week later by another injection of the same components, and booster injections given every month. Id. at 290. Eleven rabbits received bovine sciatic nerve, followed by additional injections in six rabbits every second month. Id. Sherwin followed 10 rabbits repeatedly injected with human sciatic nerve in Freund's adjuvant for three to 10 months. Id. One rabbit with mild generalized polyneuropathy developed a very severe neuropathy one week after a booster injection and died. Id. Two rabbits failed to show any signs of peripheral neuropathy although repeatedly immunized. Id. According to Figure 1, of the eight rabbits who developed symptoms, five developed symptoms within one month of inoculation with human sciatic nerve in Freund's adjuvant. A sixth rabbit had onset at one month post-inoculation. A seventh rabbit had onset at two and one-quarter months post-

inoculation. The eighth rabbit developed symptoms six and one-half months after repeated inoculations. Id. at 291.

The Saida articles have already been discussed, involving repeated injections in animals to produce EAE.

Poser and Behan return to their discussion of a vascular basis for EAE with references to articles by Waksman and Adams, Levine, and Wiśniewski and Bloom on page 31 of their article. The Waksman and Adams article is petitioner's Exhibit 81 entitled "Studies of the Effect of the Generalized Shwartzman Reaction on the Lesions of Experimental Allergic Encephalomyelitis" by B.H. Waksman and R.D. Adams, 33 Amer J Path 1:131-53 (1957). The authors induced EAE in rabbits, all of whom developed typical EAE between the ninth and 25th days post-inoculation. Id. at 132.

The Levine article is petitioner's Exhibit 44 entitled "Allergic Encephalomyelitis: Effect of Complement Depletion with Cobra Venom" by S. Levine, et al., 138 Pro Soc Exper Biol 1:285-89 (1971). The authors discuss a severe form of EAE produced in rats immunized with neural antigen and pertussis vaccine whose uniform clinical onset was seven or eight days after immunization. Id. at 285. They then induced EAE in rats through passive transfer of living, immunized lymphoid cells. Onset of clinical signs was seven days later. Id. at 288.

Poser and Behan mention toward the bottom of page 31 of their article that Behan, in unpublished observations, induced experimental allergic myasthenia gravis in animals sensitized by one immunization to the acetylcholine receptor and found, in those animals who did not develop disease, he could induce it with intravenous endotoxin, a phenomenon that occurred up to one year following immunization. He did the same to animals with EAE and EAN to the same effect. It is impossible to check these statements since they are based on unpublished

observations, but, if the experiments imitate the others already discussed where a long onset is involved, either the animals were immature (i.e., juveniles) or they had repeated injections over many months to induce EAE.

The Wiśniewski and Bloom article is petitioner's Exhibit 84 entitled "Primary Demyelination as a Nonspecific Consequence of a Cell-Mediated Immune Reaction" by H.R Wiśniewski and B.R. Bloom, 141 J Exper Med 346-59 (1975). The authors sensitized guinea pigs with killed tubercle bacilli in Freund's complete adjuvant. Four to eight weeks later, they were exposed to one of four antigens injected in their brains and then sacrificed. Id. at 347. They had primary demyelinated lesions. Id. at 348. The relevancy of these experiments was primarily to central nervous system tuberculosis and the tuberculoid form of leprosy. Id. at 356. They note that in the absence of the use of Freund's adjuvant, it is extremely difficult to induce EAE, necessitating the administration of 60-120 injections of brain homogenate to induce disease. Id. at 357.

Continuing with their thesis that GBS is a vasculopathy, Poser and Behan mention articles by Csermely, Putnam, Clark and Bailey, Garvey, Faber and Balslov, Behan, Rodriguez-Iturbe, Tachovsky, Goust, Tse, Luijten and Baart de la Faille-Kuyper, Graham, and Durward on page 32 of their article.

The article by Csermely is petitioner's Exhibit 17 entitled "Demyelinating Encephalomyelitis Following Use of Antitetanus Serum" by H. Csermely, 64 Arch Neur & Psychiat 5:676-84 (1950). Csermely discusses a case report of a man who had received tetanus vaccine, followed three days later with hives, malaise, headache, back pain, and general weakness. Id. at 677. Ten days after vaccination, he became paralyzed on the right and he lost consciousness. Id. The patient died 14 days after vaccination. Id. at 678. He had demyelination

in the white matter of his brain. Id. at 679. Csermely diagnoses this as leukoencephalitis which he characterizes as a neuroallergic reaction. Id. at 682.

The Putnam article is petitioner's Exhibit 61 entitled "Studies in Multiple Sclerosis. The Histogenesis of Experimental Sclerotic Plaques and their Relation to Multiple Sclerosis" by T.J. Putnam, et al., 97 JAMA 22:1591-96 (1931). The authors inoculated 80 dogs with tetanus toxin. Two of them developed encephalomyelitis. Id. at 1592. One dog became ataxic and weak two days after receiving tetanus toxin. Two more doses were given at weekly intervals with exaggeration of symptoms after each. After the third dose, the dog died a month after the first injection. Id. at 1592-93. The second dog received two injections of tetanus toxin and, about three weeks later, developed ataxia and spasticity. At the end of five months, he appeared perfectly well. He was then killed a year after onset of symptoms. Id. at 1593. The authors subjected 22 dogs and two cats to pure carbon monoxide. Four died at once from overdose. Two more died within a few days, showing extensive necrosis throughout their brain white matter. Of the rest, 11 never had any symptoms or lesions. Three showed areas of demyelination at autopsy performed 10, 15, and 51 days after the last exposure. Id. The authors subjected eight cats and seven dogs to cod liver oil in the hope that the oil would create emboli. Two animals died immediately. The others experienced transient paralysis occasionally. The animals were sacrificed. Four showed areas of demyelination at 20 days, one month, three months, four months, and five months after the injection of cod liver oil. Id. at 1594. The earlier lesions resembled those produced with carbon monoxide poisoning. Some of the later lesions recovered their normal appearance. Id. The authors conclude that myelin loss is permanent up to a year from the time of inoculation. Id. at 1595.

The Clark and Bailey article is petitioner's Exhibit 16 entitled "Neurological and Psychiatric Signs Associated with Systemic Lupus Erythematosus" by E.C. Clark and A.A. Bailey, 160 JAMA 6:455-57 (1956). The article concerns neurologic and psychiatric symptoms associated with lupus. Out of 100 patients, 24 had neurologic symptoms, including three with polyneuritis. Id. at 456. Two of these patients had neuronitis with elevation of protein in the cerebrospinal fluid. Id. The third patient had bilateral footdrop and absent reflexes in the lower extremities. Id. Clark and Bailey never mention GBS in their article, although Poser and Behan state at page 32 of their article that Clark and Bailey associate GBS with lupus.

The Garvey article is petitioner's Exhibit 24 entitled "Polyradiculoneuritis (Guillain-Barré Syndrome). Following the Use of Sulfanilamide and Fever Therapy" by P.H. Garvey, et al., 115 JAMA 23:1955-59 (1940). Over two years, the authors observed six cases of a syndrome resembling GBS whose onset was 10 to 16 days in five of the cases, and one month in the sixth case, after the patients received fever treatment of 15 hours. Id. at 1955-56, 1958. In three of the cases, herpes simplex virus developed. Id. at 1959. The authors assumed the fever treatment activated a virus which led to the GBS-like syndrome. Id. The most important feature of these cases which supports a viral cause of the GBS-like syndrome "was the latent period between the fever therapy and the development of the neurologic symptoms. This period was fairly uniform in the six cases reported and might well represent the incubation period of a virus present in the body which became activated by fever therapy (much as seems to be the case with the herpes simplex virus)." Id.

To simplify the rest of Poser's and Behan's arguments, the undersigned summarizes their thesis that, in laboratory animals sacrificed who had not shown clinical disease, some had signs of lesions. To Poser and Behan, this means that people who have no clinical GBS also have

subclinical lesions. They surmise on page 34 of their article that chronic relapsing polyneuritis may be a variant of acute polyneuritis. They conclude at page 38 that their theory "is only a hypothesis, however…. The value of our suggestion is that it provides an explanation for the clinical, pathological and immunological facts in GBS including those cases which have a late onset."

Respondent's Expert Submitted Material

Respondent filed as Exhibit A an article entitled "The Guillain-Barré Syndrome and the 1992-1993 and 1993-1994 Influenza Vaccines" by T. Lasky, et al., 339 NEJM 25:1797-1802 (1998). One of the co-authors is Dr. L.B. Schonberger (the author of the Schonberger swine flu-GBS epidemiological study). The authors note that after swine flu vaccination in 1976-77, the relative risk of GBS after vaccination rose for six- or eight-week periods. Id. at 1797. In subsequent flu seasons from 1978 to 1988, the authors did not find an elevated risk of GBS among vaccinees. However, in the 1990-91 flu season, they did find an elevated risk of GBS among vaccinees aged 18 to 64 years, but not in vaccinees 65 years or older. Id. They noted an increased number of GBS cases among vaccinees in the 1993-94 flu season and, for this article, did an analysis to find out if the relative risk of GBS rose over a six-week period. Id. at 1798. Comparing the rate of GBS among vaccinees in the 1993-94 flu season with that in the 1992-93 flu season, the authors found no significant difference in the effect of vaccine between the seasons. Id. at 1800. However, there was an increase of one case per million vaccinees in the 1993-94 flu season. Id. at 1801. The authors comment that the lower percentage of non-vaccine antecedent events (such as infections) in vaccine-associated GBS cases compared with the rate of antecedent infections in GBS patients who had not been vaccinated is "consistent with the

hypothesis that influenza vaccine triggered some of these cases." Id. They conclude that there was a small risk of GBS associated with flu vaccine in both 1992-93 and 1993-94. Id.

Respondent filed as Exhibit B the same article by Schonberger et al. that is petitioner's exhibit 69.

Respondent also filed 24 medical articlesas a second Exhibit A

DISCUSSION

To satisfy her burden of proving causation in fact, petitioner must prove by preponderant evidence "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Sec'y of HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

> A persuasive medical theory is demonstrated by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" the logical sequence being supported by "reputable medical or scientific explanation[,]" *i.e.*, "evidence in the form of scientific studies or expert medical testimony[.]"

In Capizzano v. Sec'y of HHS, 440 F.3d 1317, 1325 (Fed. Cir. 2006), the Federal Circuit said "we conclude that requiring either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect is contrary to what we said in Althen . . . ." Such an approach is inconsistent with the use of circumstantial evidence. *Id*.

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, 956 F.2d at 1149. Mere temporal association is not sufficient to prove causation in fact. *Id*. at 1148.

"Petitioner need not show that the vaccine was the sole or predominant cause of her injury," just that the vaccine was a substantial factor in causing her injury. De Bazan v. Sec'y of HHS, 539 F.3d, 1347, 1351 (Fed. Cir. 2008).

In essence, the special master is looking for a medical explanation of a logical sequence of cause and effect (Althen, 418 F.3d at 1278; Grant, 956 F.2d at 1148), and medical probability rather than certainty (Knudsen v. Sec'y of HHS, 35 F.3d 543, 548-49 (Fed. Cir. 1994)). To the undersigned, medical probability means biologic credibility rather than specification of an exact biologic mechanism. As the Federal Circuit stated in Knudsen:

> Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal "compensation program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." House Report 99-908, *supra*, at 3, 1986 U.S.C.C.A.N. at 6344.
>
> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others.

35 F.3d at 549.

The Federal Circuit in Capizzano emphasized that the special masters are to evaluate seriously the opinions of the vaccinee's treating doctors since "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury." 440 F.3d at 1326. See also Andreu v. Sec'y of HHS, 569 F.3d 1367, 1375 (Fed. Cir. 2009).

As the Federal Circuit stated in Knudsen, 35 F.3d at 548, "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast

per se scientific or medical rules." The undersigned's task is to determine medical probability based on the evidence before the undersigned in this particular case. Althen, 418 F.3d at1281 ("judging the merits of individual claims on a case-by-case basis").

The Federal Circuit in Knudsen, 35 F.3d at 549, also stated: "The special masters are not 'diagnosing' vaccine-related injuries."

The special masters "are entitled–indeed, expected–to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence." Moberly v. Sec'y of HHS, 592 F.3d 1315, 1325 (Fed. Cir. 2010).

Prong One of Althen

Other than incorrectly asserting that the Massachusetts and New Jersey criteria about reporting GBS support his opinion (which he admitted in his testimony they did not), Dr. Conomy testified that the sole basis for his opinion of causation is Poser's and Behan's "suggestion" that, since some people with GBS do not recover completely after they had GBS but have a smoldering course, it is logical that people with GBS might have a smoldering course before the clinical onset of their GBS began. Poser's and Behan's "suggestion" is illogical. Someone with a smoldering GBS after the acute phase has symptoms of disease. That is how the patient is diagnosed with residua of his GBS. Someone who has recovered completely from GBS does not have smoldering GBS. That patient would not be diagnosed with residua. If petitioner in the instant action had "smoldering GBS" before her acute onset, she would have had symptoms during the four months or 17 weeks between her flu vaccination and the onset of her symptoms. But she did not.

Moreover, Poser's and Behan's assertion is contrary to the diagnosis of GBS as an acute inflammatory demyelinating polyneuropathy. Petitioner does not allege that she had chronic inflammatory demyelinating polyneuropathy (CIDP) and does not assert that her onset was before four months. If Poser's and Behan's thesis were true, there would be no difference between someone who has smoldering GBS before the acute onset and someone who does not have smoldering GBS before the acute onset.

With this hypothesis, petitioner could have had smoldering GBS one year before her acute onset, which would be eight months before vaccination. Dr. Conomy testified that he was willing to opine that vaccination can cause GBS whose onset is one year later. He also testified that petitioner's onset of GBS began at some time between her flu vaccination and the clinical onset four months later, but he does not know when.

The many medical articles to which Poser and Behan refer in their hypothesis mainly show onset of demyelinating disease (either EAE or EAN) within days to weeks after an injection of human spinal cord or sciatic nerve or some neurologic antigen into an animal. Long-onset occurred in animals repeatedly injected or in immature animals. It also occurred in people who had been repeatedly injected with old anti-rabies vaccine. Petitioner in the instant action received one vaccination on December 8, 2004 followed by no more vaccinations until the onset of her GBS on April 6, 2005. Petitioner is not analogous to an immature or juvenile animal. She is 67 years old. There is no way to analogize from petitioner's receipt of one flu vaccination four months prior to onset of GBS to animal experiments in which repeated injections were administered or immature animals (juveniles) were used which resulted in a long onset to clinical disease or to analogize from petitioner's fact pattern to repeated old anti-rabies vaccinations in people.

Dr. Conomy's testimony is not only unhelpful, it also reflects medicine as it was almost 30 years ago, a similar defect in the Poser and Behan article. Dr. Whitton testified that no doctor analyzed GBS the way that Drs. Conomy, Poser, and Behan do. Dr. Conomy has an interest in the legal sphere and is board-certified in forensic medicine. He has started a corporation which enables him to testify as an expert, among the many hats he wears professionally. The impression of the undersigned is that he really is just doing a job for hire, without the commitment or experience of a neurologist in the current practice of the field such as respondent's expert Dr. Leist or an immunologist in the current practice of the field such as respondent's expert Dr. Whitton.

Dr. Charles Poser certainly had an interest in writing this article about long-onset GBS. He was testifying on behalf of plaintiffs in long-onset GBS cases in which the swine flu vaccine was allegedly the cause. Plaintiffs sued the United States under the Federal Tort Claims Act, 28 U.S.C. §§ 1346(b), 2671 et seq. after the 1976 swine flu program was instituted and then abruptly halted when there was a greater incidence of GBS among vaccinees than among baseline.

In Robinson v. US, 533 F. Supp. 320 (E.D. Mich. 1982), Dr. Poser testified that a plaintiff's GBS occurring 17 weeks after she received swine flu vaccine caused her GBS. That fact pattern is on all fours with the instant action except that plaintiff in Robinson also had an intervening cytomegalovirus. The Honorable Chief Judge Feikens ruled against plaintiff. Plaintiff's thesis through Dr. Poser and two other experts was that her onset of GBS was a few days after she received swine flu vaccine, but it smoldered for 17 weeks until she became acutely ill triggered by her cytomegalovirus. Id. at 320. Chief Judge Feikens stated that the United

States' experts "thoroughly discredited" Dr. Poser's opinion and as well as the opinions of the two other plaintiff's experts about smoldering GBS. Id. at 324. As Chief Judge Feikens stated:

> The difficulty that I have with plaintiff's case is that there is no well recognized and respected theory in the medical community that would explain the lengthy delay in onset of the GBS or substantiate any hypothesis of "smoldering" symptoms that would be "triggered" by the intervening cytomegalovirus disease. Three witnesses attempted to buttress plaintiff's theory of her late or delayed onset of GBS. Although all were qualified in their fields, the theories they presented are not presently accepted in the scientific community and I cannot question the opinions held to the contrary by so many respected scientists. In order for me to accept the opinions and hypotheses of plaintiff's experts, I must accept too many uncertainties or unknowns. In some instances, one can easily pierce the arguments posed with simple common sense.

Id. at 328.

In the almost 30 years since Dr. Poser testified and also co-authored the Poser and Behan article at issue, medicine has not supported their "suggestion" that people with GBS, an acute polyneuritis, have a smoldering course lasting up to a year after some immune challenge before their clinical symptoms become manifest. Dr. Leist, respondent's expert neurologist, testified that Poser's and Behan's suggestion of smoldering GBS before clinical onset was not in accordance with current immunologic and neurologic understanding of the nature of GBS. Dr. Poser's theory of smoldering GBS was rejected in 1982, the very year that he and Behan published their article on long-onset GBS. Just as Chief Judge Feikens could "easily pierce" with "simple common sense" the arguments plaintiff's experts in Robinson made concerning smoldering GBS, id., so too the undersigned, nearly 30 years later, finds that Dr. Poser's thesis is no more

acceptable to the scientific and medical community than it was when he offered it in court and in his and Behan's article.

Petitioner has failed to provide a persuasive medical theory connecting her flu vaccination with her GBS by a logical sequence of cause and effect showing that the vaccination was the reason for the injury. Dr. Poser's theory is not logical but contravenes modern and prevailing medical theory, his reasoning is suspect because of his involvement in swine flu litigation as a plaintiff's expert, and his reliance on outdated materials (far older than even his article) whose applicability to an elderly human who received just one vaccination and not a series of vaccinations is totally inapposite. Dr. Conomy's reliance on the Poser and Behan article, which is the total basis for his opinion, is unwarranted. "An expert's opinion is no better than the soundness of the reasons supporting it." Perreira v. Sec'y of HHS, 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994).

Prong Two of Althen

Since petitioner has failed to prove that flu vaccine can cause GBS four months later, petitioner has also failed to prove that flu vaccine did cause her GBS in this case. Petitioner has not satisfactorily proved prong two of Althen.

Prong Three of Althen

Dr. Conomy testified that petitioner's onset of GBS four months after vaccination was consistent with causation because laboratory animals can have a smoldering demyelinating disease without clinical symptoms revealed at their sacrifice and autopsy. Then Dr. Conomy switched his opinion to an unknown onset since he stated petitioner's onset would necessarily be before her clinical symptoms, but he did not know when the onset was. Petitioner cannot prove

prong three of Althen with her expert saying he does not know when the onset is because petitioner cannot prove a medically appropriate interval between vaccination and onset when the onset is unknown. If the onset were a year before her clinical GBS manifested, which is consistent with Dr. Conomy's opinion that he would accept causation one year out and he did not know when petitioner's onset was, then the onset could have occurred before petitioner received her flu vaccination. As the United States Supreme Court stated in Whitecotton v. Shalala, 514 U.S. 268 (1995), an onset occurring before vaccination cannot be a vaccine reaction.

The undersigned does not accept that a medically appropriate interval between flu vaccination and onset of GBS is four months based on the discussion for the first prong of Althen. Since Dr. Conomy does not know when petitioner's onset is, the onset may have occurred before petitioner's flu vaccination. Petitioner has not satisfactorily proved prong three of Althen.

Petitioner has not made a prima facie case of causation in fact.

CONCLUSION

This petition is dismissed with prejudice. In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court is directed to enter judgment herewith.[3]

IT IS SO ORDERED.

_____ _____

DATE Laura D. Millman
Special Master

[3] Pursuant to Vaccine Rule 11(a), entry of judgment can be expedited by each party's filing a notice renouncing the right to seek review.